

Mcl-1 GENE REGULATORY ELEMENTS
AND A PRO-APOPTOTIC Mcl-1 VARIANT

ABSTRACT OF THE INVENTION

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The present invention relates to a human Mcl-1 gene, to nucleotide sequences that act as regulatory elements for expression of an Mcl-1 gene, to polynucleotides encoding a variant Mcl-1s/ Δ TM polypeptide, and to oligonucleotides, which contain at least ten nucleotides and can hybridize specifically to a splice junction of the

10 disclosed Mcl-1 gene or to a polynucleotide encoding an Mcl-1 variant polypeptide as disclosed herein. The invention also relates to an Mcl-1s/ Δ TM polypeptide, as well as to antibodies that can interact specifically with an epitope of Mcl-1s/ Δ TM, but not with an epitope of the full length Mcl-1 polypeptide. In addition, the invention relates to a method of expressing a nucleic acid molecule in a cell by introducing into the cell

15 the Mcl-1 gene regulatory element as disclosed herein, such that a nucleic acid molecule that is operatively linked to the Mcl-1 gene regulatory element is expressed in the cell. Additionally, the present invention relates to a method of identifying an agent that can modulate expression of a nucleic acid molecule from an Mcl-1 gene regulatory element. The present invention also relates to methods of modulating

20 apoptosis of a cell, for example, by introducing an Mcl-1 gene regulatory element as disclosed herein into the cell, by introducing into the cell an Mcl-1 gene sequence as disclosed herein, or by expressing the Mcl-1s/ Δ TM polypeptide in the cell. The present invention further relates to a method of identifying a cellular factor that can be involved in splicing of an Mcl-1 gene transcript. In addition, the present invention

25 relates to a method of identifying an agent that induces expression of the Mcl-1s/ Δ TM polypeptide in a cell. The present invention also relates to a method of identifying a cell that expresses an Mcl-1s/ Δ TM polypeptide. The invention further relates to methods of treating a pathologic condition by inducing apoptosis in cells involved in the pathologic condition or by increasing viability of cells involved in the pathologic

30 condition.